methotrexate, phosphinothricin, puromycin, spectinomycin, rifampicin, and tetracyclin, and the like.

[0191] In certain embodiments gene expression is inhibited by at least 10%, preferably by at least 33%, more preferably by at least 50%, and yet more preferably by at least 80%. In particularly preferred embodiments of the invention gene expression is inhibited by at least 80%, more preferably by at least 90%, more preferably by at least 95%, or by at least 99% within cells in the pest so a significant inhibition takes place. Significant inhibition is intended to refer to sufficient inhibition that results in a detectable phenotype (e.g., cessation of larval growth, paralysis or mortality, etc.) or a detectable decrease in RNA and/or protein corresponding to the target gene being inhibited. Although in certain embodiments of the invention inhibition occurs in substantially all cells of the pest, in other preferred embodiments inhibition occurs in only a subset of cells expressing the gene. For example, if the target gene plays an essential role in cells in an insect alimentary tract, inhibition of the gene within these cells is sufficient to exert a deleterious effect on the insect.

[0192] X. Exposing Pest to dsRNA

[0193] A pest can be exposed to a dsRNA in any suitable manner that permits administering the dsRNA to the pest. For example, the pest can be contacted with the dsRNA in pure or substantially pure form, for example an aqueous solution containing the dsRNA. In one embodiment, the insect may be simply "soaked" or "sprayed" with an aqueous solution comprising the dsRNA. Alternatively, the pest may be "sprayed" with a solution comprising a dsRNA.

[0194] Alternatively, the dsRNA may be linked to a food component of the pest, such as a food component for a mammalian pathogenic pest, in order to increase uptake of the dsRNA by the insect. Ingestion by a pest permits delivery of the pest control agents to the pest and results in down-regulation of a target gene in the host. Methods for oral introduction may include, for example, directly mixing dsRNA with a, pest's food, as well as engineered approaches in which a species that is used as food is engineered to express the dsRNA or siRNA, then fed to the pest to be affected. For example, a bacteria, such as *Lactobacillus*, may be transformed with a target sequence and then fed to a pest. In one embodiment, for example, the dsRNA or siRNA molecules may be incorporated into, or overlaid on the top of, the insect's diet.

[0195] In other embodiments the pest may be contacted with a composition containing the inventive dsRNA. The composition may, in addition to the dsRNA, contain further excipients, diluents, or carriers.

[0196] The dsRNA may also be incorporated in the medium in which the pest grows or infests. For example, a dsRNA may be incorporated into a food container or protective wrapping as a means for inhibiting pest infestation. Wood, for example, may be treated with a solution comprising a dsRNA to prevent pest infestation.

[0197] In other embodiments, the dsRNA is expressed in a bacterial or fungal cell and the bacterial or fungal cell is taken up or eaten by the insect species.

[0198] As illustrated in the examples, bacteria can be engineered to produce any of the dsRNA or dsRNA constructs of the invention. These bacteria can be eaten by the insect species. When taken up, the dsRNA can initiate an RNAi response, leading to the degradation of the target mRNA and weakening or killing of the feeding insect. Alternatively, dsRNA producing bacteria or yeast cells can be sprayed directly onto the crops.

[0199] Some bacteria have a very close interaction with the host plant, such as, but not limited to, symbiotic *Rhizobium* with the *Legminosea* (for example Soy). Such recombinant bacteria could be mixed with the seeds (for instance as a coating) and used as soil improvers.

[0200] A virus such as a baculovirus which specifically infects insects may be also be used. This ensures safety for mammals, especially humans, since the virus will not infect the mammal, so no unwanted RNAi effect will occur.

[0201] Possible applications include intensive greenhouse cultures, for instance crops that are less interesting from a GMO point of view, as well as broader field crops such as soy.

[0202] This approach has several advantages, eg: since the problem of possible dicing by a plant host is not present, it allows the delivery of large dsRNA fragments into the gut lumen of the feeding pest; the use of bacteria as insecticides does not involve the generation of transgenic crops, especially for certain crops where transgenic variants are difficult to obtain; there is a broad and flexible application in that different crops can be simultaneously treated on the same field and/or different pests can be simultaneously targeted, for instance by combining different bacteria producing distinct dsRNAs.

[0203] XI. Products

[0204] The present invention provides numerous products that can encompass a dsRNA for use in controlling pests. For example, the invention provides pharmaceutical or veterinary compositions for treating or preventing a pest disease or infection of humans or animals, respectively. Such compositions comprise at least one dsRNA or RNA construct, or nucleotide sequence or recombinant DNA construct encoding the dsRNA or RNA construct, or wherein the RNA comprises annealed complementary strands, one of which has a nucleotide sequence which corresponds to a target nucleotide sequence of an pest target gene that causes the disease or infection, and at least one carrier, excipient, or diluent suitable for pharmaceutical use.

[0205] Alternatively, a pharmaceutical or veterinary composition may be used as a composition suitable for topical use, such as application on the skin of an animal or human. For example, a dsRNA may be used in a liquid composition to be applied to the skin as drops, gel, aerosol, cream, ointment, etc. Additionally, a dsRNA may be integrated into a transdermal patch or other medical device for treating or preventing a disease or condition. Other conventional pharmaceutical dosage forms may also be produced, including tablets, capsules, pessaries, transdermal patches, suppositories, etc. The chosen form will depend upon the nature of the target pest and hence the nature of the disease it is desired to treat.

[0206] Oral vaccines, for example, can be produced using the inventive constructs and methods. For example, a vaccine can be constructed by producing a dsRNA in bacteria (e.g. *lactobacillus*) which can be included in food and functions as an oral vaccine against insect infection. Accordingly, the invention provides constructs and methods for treating and/or preventing a pest disease or condition, comprising administering to a subject in need of such treatment and/or prevention, any of the compositions as herein described, said composition comprising at least one double-stranded RNA or double stranded RNA construct comprising annealed complementary strands, one of which has a nucleotide